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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Terri L. Butler et al.	Examiner:	Traviss C. McIntosh, III
Serial Number:	Not assigned	Group art unit:	1623
Filed:	23 October 2003	Docket:	BP.012US2
Title:	COMPOSITIONS AND METHODS FOR IMPROVING CARDIOVASCULAR FUNCTION		

DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA, 22313-1450

I, John A. St. Cyr, hereby declare as follows:

1. I am a joint inventor of the above referenced invention. I have received the following degrees from the University of Minnesota: BA, 1973; BS, 1975; MS, 1977; MD, 1980; Ph.D., 1988. In addition, I completed a residency in General Surgery at the University of Minnesota in 1988 and a residency in Cardiovascular Surgery at the University of Colorado in 1991. Since 1991, I have been an independent consultant in research for various companies, investigating cardiovascular methods and devices, and energy metabolism in general. Since 1995, I have consulted with Bioenergy, Inc., the assignee of this patent application, where I am Medical Director and a minority shareholder.

During the period of my master's studies, I began working in the laboratory of Dr. John E. Foker, investigating the improvement of cardiac function following myocardial bypass. Some of the findings are included in the Foker Patent (4,719,201). I have published approximately 100 scientific papers and abstracts, about 20 of which relate to ATP metabolism. Two of these papers are of record in this case.

2. In the Final Office Action in the parent case, Patent Application Serial Number

09/917,292, mailed July 15, 2003, the Examiner rejected claims 4-7 and 9 under 35 U.S.C.§ 102(b) as being anticipated by Cotter et al. and claims 1-3 and 9 and 16 under U.S.C. § 103 (b) as obvious over Cotter in view of Foker and Wakat. I make this declaration in support of the patentability of the claims in the above-identified continuing application.

3. The Examiner stated that Cotter et al teach the ingestion of eight grams of D-ribose per liter of their composition to improve cardiovascular function. Cotter et al is directed at improving the malnutrition commonly found in congestive heart failure. Cotter does not point to the ingredient ribose as being the effective component of the composition. We have found that two to ten grams of ribose, preferably five grams of ribose, taken one to four times a day, preferably at least two times a day, without the vitamins and proteins of Cotter, are sufficient to improve cardiovascular function. In order to obtain the ribose benefit, the patient would have to ingest eight ounces to two and a half quarts of the Cotter composition each day. The Examiner is asked to take notice that congestive heart patients are often restricted in the volume of liquid they are allowed to consume each day.

I was present and assisted in the research leading to the Foker patent, which is combined with Cotter in the obviousness rejection. Our aim at that time was to replenish the ATP levels of dog hearts which had been subjected to ischemic insult, as in cardiac bypass surgery. Among the methods we attempted were the intravenous, post-operative administrations of adenosine, inosine, Concanavalin A and a blocker of the enzyme adenosine deaminase. Adenine plus ribose was found to be effective. It was subsequently found that ribose alone was sufficient to enhance the replenishment of ATP. It was further noted that the ribose needed to be administered for four to five days or the ATP levels would fall again (Foker, column 7, lines 40-61). After that period, ribose administration could be discontinued and ATP levels remained normal.

During the years since these initial studies, many independent researchers have sought to make the benefits of ribose available to human patients with congestive heart failure, without success despite the ready availability of ribose. For example, Dr. Wolfgang Pliml in Germany gave 15 to 20 grams of ribose at a time to patients for up to three days and found improvement

(see specification, page 12, lines 23 et seq. from the Pliml 1992 reference). We know that so high a dosage cannot be sustained as it almost always causes gastrointestinal distress, which is often severe. We believe that this side effect has prevented the adoption of the Pliml methods. In our study, now ongoing with nearly 1000 patients with congestive heart disease and compromised systolic and diastolic function, we have found that five grams of ribose given orally at least twice a day is effective in improving cardiovascular function. We initially tested a ten gram dosage but do not now recommend the ten gram dosage. Even at the lower dosage of five grams, three woman in the study have reported diarrhea. In general, however, this regimen has been well tolerated with fewer than ten overall adverse reaction reports.

Unlike the dogs in the Foker patent, these patients do not have improvement that persists when ribose is discontinued. I attach here a paper from one of our participating doctors. The patients in this study suffered from severe congestive heart disease (Class 2 and 3) with diastolic dysfunction. By the end of the three week study, diastolic function and other parameters of cardiovascular function had improved. When the patients went off the ribose, their condition deteriorated and they requested additional supplement (personal communication). Therefore, we believe that the administration of ribose should be continuous over the course of the disease.

Preliminary studies showed a benefit of co-administration of a vasodilator, which presumably increases access of ribose to muscle tissue. Early formulations included the vitamins and cofactors claimed in the parent application which the Examiner pointed out were disclosed in Wakat. Since these patients are under close supervision of their physicians, we have found that it is not necessary to include these in the present formulation.

4. I hereby declare that all the statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issue thereon.

By: J. A. St. Cyr Date: 11/13/03

John A. St. Cyr

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Terri L. Butler et al.		
Title:	COMPOSITIONS AND METHODS FOR IMPROVING CARDIOVASCULAR FUNCTION		
Docket No.:	BP.028US2	Serial No.:	10/692338
Filed:	October 23, 2003	Due date:	
Examiner:	Traviss C. McIntosh III	Group Art Unit:	1623

Commissioner for Patents
Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Dear Sir:

Before the above referenced Patent Application is taken up for examination, please amend as follows:

Amendments to the Specification begin on page 2.

Amendments to the Claims begin on page 3.

Remarks begin on page 4.

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in this application.

Listing of claims:

Claim 1: A method for improving cardiovascular function of a subject having congestive heart failure consisting of the chronic administration of two to ten grams of D-ribose one to four times daily to the subject.

Claim 2. The method according to claim 1 further comprising the addition of an effective amount of a vasodilator .

Claim 3. The method according to claim 2 wherein the vasodilator is L-arginine, nitroglycerin, a nitrate, a nitrite, papaverine, isoproterenol, nylidrin, isoxsuprime, nitroprusside, adenosine, xanthine, ethyl alcohol, dipyramide, hydralazine, minoxiodil or diazoxide.

Claim 4. A unit dosage for improving cardiac function consisting of one to 10 grams of D-ribose; 0 to 20 grams D-glucose; one to eight grams of L-arginine; 100 to 1000 milligrams of Vitamin C; 0.1 to one milligram of Vitamin B 12 and one to 50 milligrams of Vitamin B6.

Claim 5. A unit dosage for improving cardiac function consisting of five grams of D-ribose; five grams of D-glucose; two grams of L-arginine; 500 milligrams of Vitamin C; 0.2 milligrams of folic acid; 0.25 milligrams of Vitamin B12 ad six milligrams of Vitamin B6.

Claim 6. A method of relieving the symptoms of peripheral vascular disease consisting of the administration of two to ten grams D-ribose one to four times daily to the subject for a period of at least one week.

Remarks:

The amendments to the specification do not introduce new matter, as they merely update and simplify the information in the parent specification.

The new listing of claims more distinctly point out the invention. They are supported by the parent specification. Applicant thanks the Examiner for the courtesy of an interview on November 24, 2003. Applicant's attorney presented a Declaration under 37 C.F.R. 1.132 by Applicant John A. St. Cyr, with a print out of a paper by a participating medical center. Enclosed are the original Declaration, a reprint of the paper and a copy of the Examiner's Interview Summary.

By: Kathleen R. Terry
Kathleen R. Terry
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Certificate under 37 CFR 1.1 0: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service Express Mail, mailing label number ET943088256US, in an envelope addressed to: Commissioner for Patents, Box 1450, Alexandria, VA 2313-1450 on this 13 day of January, 2004.

Signature Kathleen R. Terry